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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,234	07/03/2001	Rudolf Hauptmann	98,385-I	5009

20306 7590 10/20/2003

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EXAMINER

O HARA, EILEEN B

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 10/20/2003

17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/898,234

Applicant(s)

HAUPTMANN ET AL.

Examiner

Eileen O'Hara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☒ Certified copies of the priority documents have been received in Application No. 07511,430.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 16.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Claims 1-62 are pending in the instant application. Claims 45, 49, 56 and 58 have been amended as requested by Applicant in Paper Number 15, filed August 1, 2003.

Objection to Specification

2. The objection to the specification is withdrawn in view of Applicants' amendment.

Withdrawn Objections and Rejections

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4.2 Claims 1-62 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-59 of copending Application No. 09/898,429, for reasons of record in the previous office action. Applicants

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disagree with the Action's assertion, however, because it was a provisional rejection, Applicants elect to address this ground of rejection by submitting a Terminal Disclaimer or by argument upon notification that this rejection has been made non-provisional, all other conditions for patentability have been met, and the instant claims are otherwise in condition for allowance. The claims are still provisionally rejected.

4.1 Claims 1-62 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-44 of U.S. Patent No. 6,417,158. Although the conflicting claims are not identical, they are not patentably distinct from each other because the proteins in both applications are the same proteins and are recombinantly produced and may or may not be glycosylated, and the methods of treatment are with the same proteins.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 15-22 and 45-62 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5.1 Claims 15-22, 45-48 and 50-62 remain rejected under 35 U.S.C. 112, second paragraph, for reasons of record in the previous office action, Paper No.13, at page 5.

Applicants traverse the rejection and assert that the claims contain an explicit limitation to encompass only those molecules that possess the ability to bind TNF, and that one of ordinary skill in the art would readily recognize that a molecule having conservative substitutions at every

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amino acid position would lack high affinity TNF- α binding activity, and that 35 U.S.C. 112, second paragraph, only requires that one of ordinary skill in the art would be able to determine which species fall within the scope of the claim.

Applicants' arguments have been fully considered but are not deemed persuasive. As written, the claims encompass proteins that can have extensive structural differences from the proteins disclosed, and additionally there is no limitation that the claimed molecule bind TNF- α with "high affinity", only that the molecule has the ability to bind TNF- α . The claims are considered indefinite, since they do not clearly set forth the metes and bounds of the patent protection desired, and the rejection is maintained.

5.2 Claim 49 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record in the previous office action, Paper No.13, at page 5.

Applicants have amended claim 49 to include hybridization conditions that are disclosed in the specification. However, the washing conditions are also a crucial part of the hybridization process and the results obtained. This rejection would be overcome by including wash conditions disclosed in the specification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 15-22, 45-48 and 50-62 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using a polypeptide comprising

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the amino acid sequence of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18 and 20 identified as TNF receptor, does not reasonably provide enablement for making and using polypeptides that have at least one conservative amino acid substitution, substitution at a glycosylation site, substitution at a proteolytic cleavage site, substitution at a cysteine residue, amino acid deletion, insertion, or combinations of the above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claims 15-22, 37-40, 43-48 and 50-62 also remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record in the previous Office Action, Paper No. 13, at pages 6-10.

Claims 37-40, 43 and 44, encompassing C- and/or N-terminally shortened sequences were mistakenly included in the rejection, but are not rejected under 35 U.S.C. 112, first paragraph.

Applicants traverse the rejection and assert that the specification sets forth the amino acid sequence of a TNF receptor polypeptide and teaches the TNF binding portion, signal peptide and that amino acid residues 30-40 and 202-211 are proteolytically cleaved from the TNF receptor to form the TNF binding protein, and that they are under no duty under the statute to enumerate all of the species disclosed generically in their specification, particularly where the structure of the native molecule is disclosed, the types of variants of said structure are generically disclosed, and a functional property of the claimed molecule and assays to assess for species for said property are disclosed. Applicants also assert that the specification teaches the location of glycosylation sites, proteolytic cleavage sites, and cysteine residues, wherein amino acid substitutions can be made. Applicants also disagree with the Action's assertion that the claims of the instant

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application are analogous to claim 7 of U.S. Patent No. 4,703,008, because the disclosure was limited to only a few erythropoietin variants while the claim encompassed over a million different erythropoietin variants, and in contrast, the instant application discloses a 161 amino acid portion of the TNF receptor polypeptide that possesses the ability to bind TNF, specific sites, and a list of exemplary conservative substitutions. Applicants also note that the independent claims contain an explicit limitation to encompass only those molecules that possess the ability to bind TNF, and disagree with the examiner's assertion regarding the specie of substituted molecule having conservative substitutions at every amino acid position.

Applicants arguments pertaining to changes at glycosylation sites, proteolytic sites and cysteine residues are persuasive, because there are a limited number of changes that can be made and tested, and these sites are disclosed in the specification. However, Applicants' arguments have been fully considered but are not deemed persuasive for TNF binding proteins having unlimited numbers of conservative amino acid substitutions, also in combination with unlimited insertions and deletions. Because of the lack of structure encompassed by the claims, undue experimentation would be required to make and test all of the possible proteins. The written description guidelines indicate that a representative species may be adequately described through its structure, through its functional characteristics, or through a combination of its structure and function. Although there is a functional limitation in the claims, many of the claims encompass proteins that can differ extensively from the disclosed amino acid sequence. The claims do not provide adequate structure to meet the written description guidelines. Therefore, the rejection is maintained.

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It is believed that all pertinent arguments have been answered.

Pertinent Art

7. The art considered pertinent to the present application is Corti et al., Journal of Interferon and Cytokine Research, Vol. 15, pages 143-152 (1995), which teaches that the soluble urinary protein of the TNF receptor type I (the same proteins as those in the instant claims) are glycosylated differently from the same protein produced recombinantly by CHO cells, and have a different activity when produced recombinantly by *E. coli* cells (nonglycosylated form). Therefore, recombinantly produced soluble TNF receptor is distinct from that of naturally occurring soluble TNF receptor.

Conclusion

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

A handwritten signature in cursive script that reads "Eileen B. O'Hara". The signature is written in black ink and is positioned below the printed name.

Patent Examiner